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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/214,913	03/16/1999	RICHARD ANTHONY GODWIN SMITH	033236/0110	8029

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 04/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,913	SMITH ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-17,19-24,26-28,35-37,41,44,47 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 13-17, 19-24, 26-28, 35-37, 41, 44, 47 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

4) ☐ Interview Summary (PTO-413) Paper No(s).

DETAILED ACTION

1. Claims 1-11, 13-17, 19-24, 26-28, 35-37, 41, 44, 47 and 50 are pending.

2. In view of the amendment filed 1/28/02, the following rejections remain.

3. Claims 1-11, 13-17, 19-20, 23, 26-28, 35-37, 41, 44 and 47 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention for the same reasons set forth in Paper No 13.

Applicants' arguments filed 1/28/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the table of therapeutic proteins on page 5 of the specification lists a selection of "soluble polypeptides" with known therapeutic properties and (2) the soluble polypeptides described in examples cover several wide-ranging categories of proteins.

However, other than the specific soluble polypeptide consisting of only two membrane binding elements wherein one the membrane binding elements is a myristoyl fatty acid with 12 methylene units and a basic polylysine amino acid sequence selected from the group consisting of GSSKSPSKKKKKKPGD, DGPKKKKKKSPSKSSG, SPSNETPKKKKKKRFSFKKSG, DGPKKKKKKSPSKSSK, SKDGKKKKKKSKTK, DGPKKKKKKSPSKSSGC, GSSKSPSKKKKKKPGDC, CDGPKKKKKKSPSKSSK, or SKDGKKKKKKSKTKC which is covalently associated with a soluble complement receptor (SCR1-3) (SEQ ID NOS: 7-14 and 17), or a conjugate of Streptokinase (SEQ ID NO: 21), or a plasminogen activator (SEQ ID NO: 22) for in vitro assays, there is insufficient written description about the structure associated with functions of (1) *any* "soluble derivative" of *any* "soluble polypeptide" wherein said "soluble derivative" comprising two or more "membrane binding elements" wherein the binding elements are not all identical as recited in claim 1 and selected from the group consisting of (2) *any* "fatty

[illegible] "complement inhibitors from complement regulatory proteins" and "hybrids" or "mutems

thereof" as recited in claims 13 and 19; (6) *any* "fragment" of soluble CR1 polypeptide as recited in claim 19-20 and 44, (7) *any* "thrombolytic agent" as recited in claim 23 and 47, *any* "derivative" as recited in claims 26-28, 37, since the base claim 1 requires at least two or more membrane binding elements covalently associated with a polypeptide and *any* "compound" as recited in claim 36. There is also a lack of written description about (8) *any* "chemical bridging groups "-A-R-B-" associated with *any* soluble derivative as recited in claims 16-17 since the base claim 1 requires the polypeptide be "covalently linked" with two or more membrane binding elements.

The specification discloses only a soluble derivative of a soluble polypeptide consisting of only two heterologous membrane binding elements wherein one the membrane binding elements is a myristoyl fatty acid with 12 methylene units and a basic polylysine amino acid sequence selected from the group consisting of GSSKSPSKKKKKKPGD, DGPKKKKKKSPSKSSG, SPSNETPKKKKKKRFSFKKSG, DGPKKKKKKSPSKSSK, SKDGKKKKKKSKTK, DGPKKKKKKSPSKSSGC, GSSKSPSKKKKKKPGDC, CDGPKKKKKKSPSKSSK, or SKDGKKKKKKSKTKC which is covalently associated with a soluble complement receptor (SCR1-3) (SEQ ID NOS: 7-14 and 17), or a conjugate of Streptokinase (SEQ ID NO: 21), or a plasminogen activator (SEQ ID NO: 22) for **in vitro assays** such as inhibition of complement-mediated lysis (pages 50-52), plasminogen activator assay (page 53) and erythrocyte binding assays (See pages 54-57).

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.* Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

4. Claims 1-11, 13-17, 19-20, 23, 26-28, 35-37, 41, 44 and 47 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

persuasive

Applicants' position is that (1) the term "thermodynamic additivity" is well known in the art and applicants provided several related references on "additivity"; (2) when a "linker" is used, the membrane binding elements would still be linked "covalently" and those skilled in the art would understand that elements could be either spaced apart or linked together directly. However, the specification as filed does not define the term "thermodynamic additivity". The recitation of "**thermodynamic additivity**" in claim 1 renders the claim ambiguous and indefinite because one of ordinary skill in the art cannot appraise the metes and bounds of the term "**thermodynamic additivity**" since the specification does not defines the term.

The recitation of "a flexible linker group" in claim 14 and "linker group" in claim 15 is indefinite and ambiguous because base claim 1 requires the binding elements to be "covalently" associated.

5. Claims 1-3, 5-10, 14-15 and 26 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sigal *et al*, (of record, Proc. Natl. Acad. Sci. USA 91: 12253-12257, Dec 1994; PTO 892) for the same reasons set forth in Paper No 13.

Applicants' arguments filed 1/28/02 have been fully considered but are not found persuasive.

Applicants' position is that Sigal et al describes the phenomenon of thermodynamic additivity between hydrophobic and electrostatic interactions mediated by myristoyl and basic peptide residues in the protein Scr and Scr is an intracellular protein which does not normally exist in a soluble form outside the cell and that the modification with myristoylated basic peptides to soluble extracellular proteins could not be deduced from the data described by Sigal et al.

However, the myristoyl group and basic peptide residues such as lysine are well known membrane anchored elements for anchoring any protein to the membrane as evidence by Sigal *et al*. Further, Sigal *et al* teach these myristoyl and basic peptide residues are capable of interacting with each other as applicant stated on page 12 of the amendment filed 1/28/02. Sigal *et al* teach how to measure the interaction of soluble polypeptide such as Scr using artificial membrane such as liposome in fluids, which is extracellular. Sigal *et al* teach a membrane targeting motif consists of myristoyl group (Myr) and a hydrophilic amino acid sequence rich with positively

vesicles (artificial membrane) with an apparent dissociation constant Kd of 10^{-} M (low

membrane affinity) whereas a peptide containing five basic residues binds to phosphatidycholine/phosphatidyserine (artificial membrane) with a Kd of 10^{-3} M (low membrane affinity). However, a peptide containing both the myristoyl group (Myr) and the amino acid sequence rich in positively charged amino acid residues such as lysine residues that bind to membrane with a Kd of 10^{-7} M, indicating that the hydrophilic and electrostatic binding energy are additive (see page 12253, column 2, in particular). Claims 14-15 are included in this rejection because the linker group as defined in the specification could be any unspecified amino acids that forms a peptide bond which reads on the prior art.

Because the reference membrane binding elements have the same structure as the claimed membrane binding elements, the binding properties of the reference membrane binding elements (myristate and lysine) are inherent. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Claim 3 is included in this rejection because each membrane binding element is small, with a maximum number of 20 amino acids for the peptidic binding element wherein each amino acid residue is roughly equal to about 100 Dalton, which is about 2 kDa (20 x 100 = 2,000 or 2 kDa) and the molecular weight of a myristic fatty acid which is about 228. The combine membrane elements have a molecular weight of less than 5kDa. Claim 5 is included in this rejection because lipid and high ionic strength (salt) solution are known for their use as a pharmaceutical carrier because of their solubility. The peptidic membrane binding element (basic amino acid sequence) is located at the N terminus of the soluble polypeptide linking together via a peptide bond. The transitional phrase "comprising" in claim 1 is open-ended. It opens up the claims to read on additional amino acid residues. Thus, the reference teachings anticipate the claimed invention.

6. Claims 1-3, 6-11, 14-15 and 26 stand rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 5,776,689 (of record, filed July 1996, PTO 892) for the same reasons set forth in Paper No 13.

Applicants' arguments filed 1/28/02 have been fully considered but are not found persuasive.

[illegible] produced, would bind to the outer cell surface

However, applicants argue limitations "fusion protein" and "binding to the outer cell surface" which not recited in the claims.

The '689 patent teaches a fusion polypeptide consisting of two heterologous membrane binding elements (Myristyolation signal, M) and a basic amino acid sequence which is rich in lysine residues covalently associated with a polypeptide wherein the membrane elements are fatty acid derivative such as the Myristoyl group of the myristic fatty acid which has low membrane binding affinity and a basic amino acid sequence SKDGKKKKKKSKTKCVIM (See Figure 1, column 8 line 57, SEQ ID NO: 2 of '689, column 10, line 3-7, in particular). The said fatty acid is from aliphatic acyl group with about 12 methylene units and the basic amino acid sequence includes 6 lysine (K) residues, which is within the range of n equal to about 3 to 10. The peptidic membrane binding element (basic amino acid sequence) is located at the N or the C terminus of the soluble polypeptide linking together via a peptide bond (See Fig 1, in particular). The derivative has at least one element is hydrophilic (polylysine) and comprises at least two membrane binding elements which are the fatty acid and polylysine basic amino acid sequence. The transitional phrase "comprising" in claim 1 is open-ended. It opens up the claims to read on additional amino acid residues. The '689 patent further teaches that a fusion protein containing one of the membrane binding elements will localize the fusion protein to the plasma membrane (See column 8, lines 65-67 bridging column 9, lines 1-2, in particular). Because the reference membrane binding elements have the same structure as the claimed membrane binding elements, the binding properties of the reference membrane binding elements (myristate and lysine) are inherent. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Claim 2 is included in this rejection because of the inherent properties of each binding element is low membrane affinity. Claim 3 is included in this rejection because each membrane binding element is small, with a maximum number of 20 amino acids for the peptidic binding element wherein each amino acid residue is roughly equal to about 100 Dalton, which is about 2 kDa (20 x 100 = 2,000 or 2 kDa) and the molecular weight of a myristic fatty acid which is about 228. The combine membrane elements have a molecular weight of less than 5kDa. Claims 14-15 are included in this rejection because the linker group as defined in the specification [illegible]

[illegible]

7. Claims 1, 13, 19-20, 37, 41 and 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sigal *et al*. (of record. Proc. Natl. Acad. Sci. USA 91: 12253-12257, Dec 1994; PTO 892) in view of US Pat No. 5,472,939, (Dec 1995, PTO 892) for the same reasons set forth in Paper No 13.

Applicants' arguments filed 1/28/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) there is no motivation at the time the invention was made to combine the binding elements identified by Sigal et al with the soluble form of CR1 as taught by the '939 patent; (2) the large increases in potency observed when applying the modifications of the present invention were quite unexpected.

However, arguments of counsel cannot take the place of evidence.

The teachings of Sigal *et al* have been discussed supra.

The claimed invention of claim 13 differs from the references only by the recitation of the soluble polypeptide is a complement inhibitor.

The claimed invention of claim 19 differs from the references only by the recitation of the soluble polypeptide is a soluble complement inhibitor.

The claimed invention of claim 20 differs from the references only by the recitation of the soluble polypeptide is a soluble CR1 polypeptide fragment.

The claimed invention of claim 37 differs from the references only by the recitation of a pharmaceutical composition comprising a derivative of claim 1 in combination with a pharmaceutical acceptable carrier.

The claimed invention of claim 41 differs from the references only by the recitation of a pharmaceutical composition for treating a disease or disorder associated with inflammation or inappropriate complement activation comprising a therapeutically effective amount of a derivative of a soluble complement inhibitor and a pharmaceutically acceptable carrier or excipient.

The claimed invention of claim 44 differs from the references only by the recitation of a pharmaceutical composition for treating a disease or disorder associated with inflammation or inappropriate complement activation comprising a therapeutically effective amount of a [illegible]

The '939 patent teaches a soluble complement regulatory protein sCR1 which has a short consensus structure motif that binds to a complement component for reducing tissue damage associated with myocardial infarction (See column 8, lines 15-40, column 9, lines 29 and 43-44, column 67, 68, 69 and Abstract, in particular). The '939 patent further teaches a fusion protein comprising a portion of the CR1 sequence plus a non-CR1 sequence (See column 21, lines 39-42). The '939 patent teach other deletion mutants of CR1 which are functional derivatives (See column 16, lines 41-58, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to covalently link the binding elements as taught by Sigal *et al* with the soluble complement inhibitor for a pharmaceutical composition consisting of a soluble derivative of a soluble complement comprising two or more heterologous membrane binding elements wherein the binding elements are a basic amino acid sequence and a myristoyl group covalently associated with the soluble complement receptor (CR1) or a functional derivative thereof.

One having ordinary skill in the art would have been motivated to use a soluble complement receptor inhibitor which is a soluble (CR1) peptide fragment or a functional derivative as taught by the '939 patent because the '939 patent teaches that a soluble CR1 molecule or fusion protein may be used to treat damage caused by a myocardial infarction associated with inflammation and inappropriate complement activation (See column 8, lines 15-40, column 9, lines 29 and 43-44, column 67, 68, 69 and Abstract, in particular). Sigal *et al* teach that a peptide containing both the myristoyl group (Myr) and the positively charged lysine residues can enhance the binding of the soluble polypeptide to the membrane because the hydrophilic and electrostatic binding energy are additive (see page 12253, column 2, in particular).

8. Claims 1, 13, 23-24, 37, 47 and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sigal *et al*, (of record, Proc. Natl. Acad. Sci. USA 91: 12253-12257, Dec 1994; PTO 892) in view of EP 0,207,589 A1, (Jan 1987, PTO 892) or EP 0,155,387 A2 (Sept 1985, PTO 892) or US Pat No 5,326,700 (July 1994, PTO 892) for the same reasons set forth in Paper No 13.

Applicants' arguments filed 11-28-02 have been fully considered but are not found

Applicants' position is that (1) none of the references (the '589 patent and the '387 patent, the '736 and the '700 patent teach that directing a fibrinolytic agent to a cell membrane would be useful in treatment of thrombosis nor do they suggest a means of achieving this end.

However, Sigal *et al* teach the specific membrane binding elements that have been discussed supra.

The claimed invention of claim 13 differs from the references only by the recitation of the soluble polypeptide is a prourokinase, streptokinase, or tissue-type plasminogen activator.

The claimed invention of claim 23 differs from the references only by the recitation of the soluble polypeptide is a thrombolytic agent.

The claimed invention of claim 24 differs from the references only by the recitation of the soluble polypeptide is a SEQ ID NO: 22, which is a tissue plasminogen activator.

The claimed invention of claim 37 differs from the references only by the recitation of a pharmaceutical composition comprising a derivative of claim 1 in combination with a pharmaceutical acceptable carrier.

The claimed invention of claim 50 differs from the references only by the recitation of a pharmaceutical composition for treating thrombotic disorders comprising a therapeutically effective amount of a soluble derivative of SEQ ID NO: 22.

The claimed invention of claim 47 differs from the references only by the recitation of a pharmaceutical composition for treating thrombotic disorders comprising a therapeutically effective amount of a derivative wherein the derivative is prourokinase, streptokinase or tissue-type plasminogen activator and a pharmaceutically acceptable carrier or excipient.

The EP 0207,589 A1 patent teaches tissue type plasminogen activator, functional derivatives thereof such as urokinase (see page 10, in particular) and pharmaceutical compositions for treatment of thrombotic diseases (See page 6, lines 39-42).

The EP 0,155,387 A2 patent teaches hybrids of plasmin linked to urokinase plasminogen activator B-chain (See page 11, claims 1-4 of EP 0,155,387 A2 and a pharmaceutical composition for treating thrombotic diseases (See pages 6-7, in particular).

The '700 patent teaches a tissue plasminogen activator having an amino acid sequence identical to SEQ ID NO: 22 of the instant application (See claims 39, SEQ ID NO: 16 of '700 in

invention was made to covalently link the membrane binding elements as taught by Sigal *et al*

with the tissue type plasminogen activator, or functional derivatives thereof such as urokinase as taught by the EP 0207,589 A1 patent or the hybrids of plasmin linked to urokinase plasminogen activator B-chain as taught by the EP 0,155,387 A2 patent or the tissue plasminogen activator as taught by the '700 patent for a soluble derivative comprising the myristoylated basic amino acid sequence covalently linked to a tissue type plasminogen activator, tissue factor, urokinase plasminogen activator for treating thrombotic disease.

One having ordinary skill in the art would have been motivated to use the tissue type plasminogen activator, or functional derivatives thereof and hybrid as taught by the EP 0207,589 A1 patent or the EP 0,155,387 A2 patent or the plasminogen activator as taught by the '700 patent because the said soluble plasmin, derivative and hybrids thereof, or the plasminogen activator can be used for treating thrombotic disease. Sigal *et al* teach that a peptide containing both the myristoyl group (Myr) and the positively charged lysine residues can enhance the binding of the soluble polypeptide to the membrane because the hydrophilic and electrostatic binding energy are additive (see page 12253, column 2, in particular).

9. Claims 1 and 14-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sigal *et al*, (of record, Proc. Natl. Acad. Sci. USA 91: 12253-12257, Dec 1994; PTO 892) in view of EP 0152736 A2 (Aug 1985; PTO 892) for the same reasons set forth in Paper No 13.

Applicants' arguments filed 1/28/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) none of the references (the '589 patent and the '387 patent, the '736 and the '700 patent teach that directing a fibrinolytic agent to a cell membrane would be useful in treatment of thrombosis nor do they suggest a means of achieving this end.

However, Sigal *et al* teach the specific membrane binding elements which have been discussed supra.

The combined teachings differ from the claimed invention by not using the chemical bridging groups having the formula (I): -A-R-B- in which each of A and B, which may be the same or different, represents -CO-, -C(=NH2+)-, maleimido, -S-, or a bond and R is a bond or a

q are independently integers of at least 2, or (CH2)2CONH(CH2)nNH-(4-phenyl) where n is an integer of 3 to 8.

The EP 0152736 patent teaches an enzyme-protein conjugate using bridging groups having a formula of (I): -A-R-B- in which each of A and B, which may be the same or different, represents -CO-, -C(=NH2+)-, maleimido, -S-, or a bond and R is a bond or a linking group containing one or more -(CH2)- or meta-, ortho- or para- disubstituted phenyl units optionally together with a hydrophobic portion; the R is selected from -(CH2)r-, -(CH2)p-S-S-(CH2)q- (See pages 2-3, 31, in particular). The EP 0152736 patent further teaches the enzyme-protein conjugates made using the method mentioned above are suitable as a pharmaceutical composition (See page 11, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the covalently link heterologous membrane binding elements with a soluble polypeptide as taught by Sigal *et al* with a chemical cross linking group as taught by the EP 0152736 patent for a soluble peptide derivative.

One having ordinary skill in the art would have been motivated to use the bridging group as taught by the EP 0152736 patent because the derivative or conjugates made using these bridging group are suitable for pharmaceutical compositions (See page 11, in particular).

10. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. [illegible]

[illegible] left on the examiner's voice mail service. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
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April 22, 2002

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